REMARKS

I. Preliminary Remarks

A petition under 37 C.F.R. § 1.81 and § 1.144 was filed on March 15, 2004, which requested review and withdrawal of a 442-way restriction requirement. The decision, mailed on October 27, 2004, granted the petition in part. The original restriction requirement mailed September 19, 2002 was withdrawn and a new restriction was set out in the decision[1]. This amendment is a response to the new restriction requirement.

By this amendment, all claims pending at the time of the new restriction requirement are canceled, solely for the purpose of providing a consecutively numbered set of claims consistent with the Applicants' election. The Applicants reserve the right to pursue the same or similar subject matter of any canceled claim in a continuing application.

Some of the new claims recite particular peptide sequences which are supported by the specification. For example, peptides SEISY-EVEFR (SEQ ID NO: 152; claims 110 and 135), SEVSY-EVEFR (SEQ ID NO: 141; claim 114), KTEEISEVSY-EVEFR (SEQ ID NO: 147; claims 115), and TRPGSGLTNIKTEEISEVSY-EVEFR (SEQ ID NO: 145; claims 116) are supported in Table 5 at page 25 of the specification. Peptide SEISY-EVEFRWKK (SEQ ID NO: 190; claims 112) is supported at page 26, line 28. Peptide GLTNIKTEEISEISY-EVEFRWKK (SEQ ID NO: 191; claims 113) is supported at page 26, line 27. The peptides encompassed by the recitation in claim 117 are supported at page 19, lines 8-11, and page 23, lines 7-11. A substrate that comprises an APP amino acid sequence with a modified β-secretase processing site, as recited in claim 118, is supported at page 8, lines 4-8. Claim 130 recites a transgenic non-human mammal, which is supported at pages 67-74.

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[1] The reformulated restriction requirement is objectionable because it does not follow Patent Office guidelines in the MPEP or the recently promulgated Group 1600 training materials for interpreting the MPEP. For example, it is a facial violation of the *PTO's burden of demonstrating distinctness* to allege that 2940 peptides fall within 2940 restriction groups, in the absence of a pairwise analysis of the 2940 groups. Using the formula and table employed to "calculate" the restriction groups, every peptide defined by P2P1-P1'P2' shares 3 of its four residues in common with twenty-seven other peptides, and in most instances, one or more of those twenty-seven neighbors differs by way of a conservative substitution. No reasoning or evidence is presented as to why such peptides are all distinct from each other. (Compare the Group 1600 training materials, where the guidelines DID NOT RESTRICT each member of a class of humectants (Group 1610/20 Example 1, claims 2, 8); emollient (claims 3, 9), aromatherapeutical (claim 10), "soothing substance" (claim 20), even though there

The amendment to the specification to insert several paragraphs of text finds support in U.S. patent application no. 09/416,901 (now U.S. Patent No. 6,699,674) at page 9, line 19, through page 10, line 12, at page 33, line 7-23 and at page 50, line 20, through page 51, line 12 . This patent application is incorporated by reference in its entirety in the present application (see page 39, lines 26-27). Therefore, insertion of these paragraphs does not add new matter to the specification pursuant to 37 C.F.R. 1.57(c).

The substitute sequence listing includes the murine Asp2 polynucleotide (SEQ ID NO: 198) and polypeptide (SEQ ID NO: 199) sequences. These sequences are referred to in the paragraphs that are incorporated by reference by the foregoing amendment. The substitute sequence listing does not add new matter to the specification pursuant to 37 C.F.R. § 1.57(c).

A number of the claims contain limitations defining the beta secretase polypeptide used in methods of the invention. These claim recitations are described in the specification at page 39, line 18 through page 42, line 4, including the paragraphs newly introduced from the application that is incorporated by reference. (In addition, these polypeptides and polynucleotides are claimed in related U.S. Patent Nos. 6,828,117, 6,825,023, 6,737,373, 6,797,487, 6,753,163 and allowed U.S. Patent Applications Nos. 09/548,365 and 09/548,370.)

II. Restriction and Election

Pending claim 1-101 were restricted into the following groups of inventions. The Applicants were required to elect (1) a particular type of invention and (2) a particular peptide used in or referred to by the invention.

A. Groups 1-2940: Claims 1-23, 25-35 and 70-101 are drawn to a peptide which comprises an amino acid sequence with the formula P2 P1 P1' P2' wherein P2, P1, P1' and P2' are each selected from the amino acid residues set forth in the table below.

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was no common chemical structure for the members of these groups. See also Group 1630/40 Example 1, where the PTO did NOT separately restrict every nucleic acid of unique sequence that fell within claim 1.

P2	P1	P1'	P2'
N	Y	E	V
L	L	A	A
K	M	D	N
S	Nle	M	T
G	F	Q	L
T	H	S	F
D		G	S
A			
Q			
E			

B. Groups 2941-5430: Claims 36-42 and 52-54 are drawn to a polynucleotide that encodes one of the polypeptides of Groups 1-2940, a vector, host cell and a method of producing a substrate for a β-secretase assay.

C. Groups 5430-8370: Claims 43-48, 50, 58-64 and 66-67 are drawn to a method for assaying for modulators of β-secretase activity, identifying agents that inhibit Asp2 aspartyl protease or modulate the Asp2 aspartyl protease using a peptide of Groups 1-2940.

D. Groups 8370-11,310: Claims 49, 51, 55-57, 65 and 68-69 are drawn to a method of inhibiting the β-secretase activity *in vivo* comprising administering a modulator identified using a peptide of Groups 1-2940, a pharmaceutical composition comprising a modulator, a method of treating a disease comprising administering the pharmaceutical composition and the use of a modulator to treat Alzheimer's disease.

Applicants hereby elect the invention drawn to methods for assaying for modulators of β-secretase activity (Groups 5430-8370) using the peptide having the particular amino acid sequence SYEV. All of the new claims are believed to correspond with the elected subject matter. Claims 102-109 and 117-131 are all generic linking claims. According to MPEP §809.04 and the decision that reformulated the restriction requirement,

the generic linking claims should be examined along with the examination of the method claims that use a peptide comprising the amino acid sequence SYEV (claims 110-116)

CONCLUSION

In view of the above amendment, Applicants believe pending claims 102-131 are in condition for allowance.

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Respectfully submitted,

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